

Formula 1

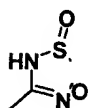
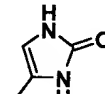
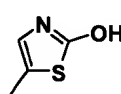
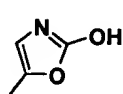
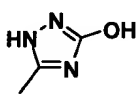
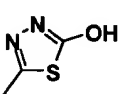
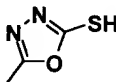
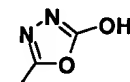
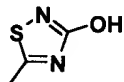
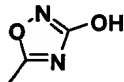
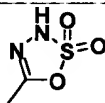
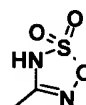
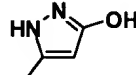
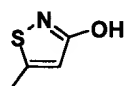
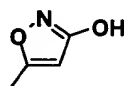
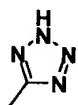
wherein

n is 1 or 2;

m is 1 or 2;

Y is O, S, SO or SO₂;

R₁ is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl or a 5-membered heterocycles selected from the group consisting of:



R₂ is hydrogen;

R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₄ is hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined below;

C₁
Methyl

R₅, and R₆ are independently hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxycarbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylaminoC₁-C₆alkyl, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₈C₁-C₆alkylCOR₁₀, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, C₁-C₆alkylCONR₇R₈ or arylaminocarbonylaminoC₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined below and R₁₀ is NR₇R₈, or C₁-C₆alkylNR₇R₈;

R₇ and R₈ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy wherein the alkyl and aryl groups are optionally substituted as defined in the section of definitions; or R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic monocyclic, bicyclic or tricyclic ring system containing from 3 to 14 carbon atoms and from 0 to 3 additional heteroatoms selected from nitrogen, oxygen or sulphur, wherein the ring system is optionally substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylaminoC₁-C₆alkyl or NR₁₁R₁₂, wherein R₁₁ and R₁₂ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted as defined below; or

R₇ and R₈ are independently a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam;

wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo, COOR₃, CONR₇R₈, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, NR₇R₈, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy, arylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-C₆alkylaminoCOR₁₃, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, -CONR₇R₈, -C₁-C₆alkylCONR₇R₈, or a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam, wherein R₁₃ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy;

and wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, CONR₇R₈, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, -arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₇C₁-C₆alkylCOR₁₃, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆-alkylcarbonylaminoC₁-C₆alkyl, -CONR₇R₈, or -C₁-C₆alkylCONR₇R₈.

111. (new) The compound according to claim 110, wherein R₁ is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl or COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl.

112. (new) The compound according to claim 110, wherein n and m are 1.

113. (new) The compound according to claim 110, wherein Y is oxygen.

114. (new) The compound according to claim 110, wherein R₁ is 5-tetrazolyl, R₅ is C₁-C₆alkylNR₇R₈ and Y is oxygen.

115. (new) The compound according to claim 110, wherein R₄ and R₆ are hydrogen.

116. (new) The compound according to claim 110, wherein R₆ is C₁-C₆alkylNR₇R₈.

117. (new) The compound according to claim 110, wherein the aryl group is pyridyl

118. (new) The compound according to claim 110, wherein the aryl group is phenyl optionally substituted with methoxy or CH₃C(O).

119. (new) The compound according to claim 110, wherein R₇ is hydrogen and R₈ is C₁-C₆alkylaryl.

120. (new) The compound according to claim 110, wherein R₆ is arylaminocarbonylaminoC₁-C₆alkyl.

121. (new) The compound according to claim 110, wherein R₆ is aryloxyC₁-C₆alkyl.

122. (new) The compound according to claim 110, wherein the aryl group is 1,1-dioxo-benzo[d]isothiazol-3-yl.

123. (new) the compound according to claim 110, wherein the aryl group is 1,1-dioxo-5-phenyl-isothiazol-3-yl.

124. (new) The compound according to claim 110, wherein the aryl group is benzo[1,3]dioxol-5-yl.

125. (new) The compound according to claim 110, wherein the aryl group is 5-methoxy-2-methyl-1H-indol-3-yl.

126. (new) A composition comprising an effective amount of a compound of claim 110, together with one or more pharmaceutically acceptable carriers or diluents and an insulin sensitizer.

127. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 110 and an insulin sensitizer.

128. (new) A composition comprising an effective amount of a compound of claim 110, together with one or more pharmaceutically acceptable carriers or diluents and an agent stimulating insulin release from β cells.

129. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 110 and an agent stimulating insulin release from β cells.

130. (new) A composition comprising a compound of claim 110, together with one or more pharmaceutically acceptable carriers or diluents and an antiobesity agent.

131. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 110 and an antiobesity agent.

132. (new) A composition according to claim 126, wherein the insulin sensitizer is a thiazolidinedione or a pharmaceutically acceptable salt thereof.

133. (new) A composition according to claim 126, wherein the insulin sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione and 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salts thereof.

134. (new) A composition according to claim 126, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

135. (new) The method according to claim 127, wherein the insulin sensitizer is a thiazolidinedione or (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

136. (new) The method according to claim 127, wherein the insulin sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione or (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

137. (new) The method according to claim 127, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

138. (new) A composition according to claim 128, wherein the agent stimulating insulin release from β cells is repaglinide.

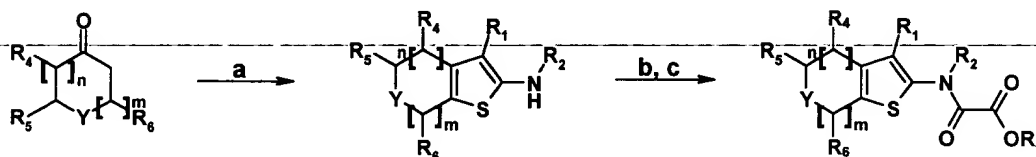
139. (new) The method according to claim 129, wherein the agent stimulating insulin release from β cells is repaglinide.

140. (new) A composition according to claim 130, wherein the antiobesity agent is orlistat.

141. (new) The method according to claim 131, wherein the antiobesity agent is orlistat.

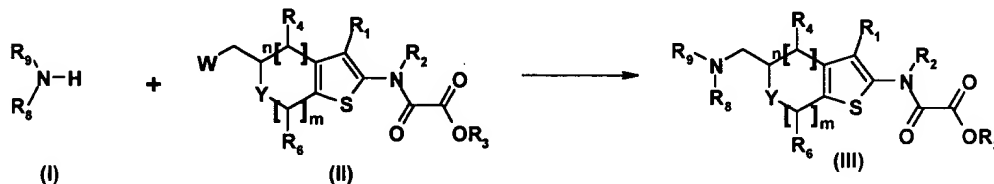
142. (new) A method for preparing the compound of claim 110, comprising

A)



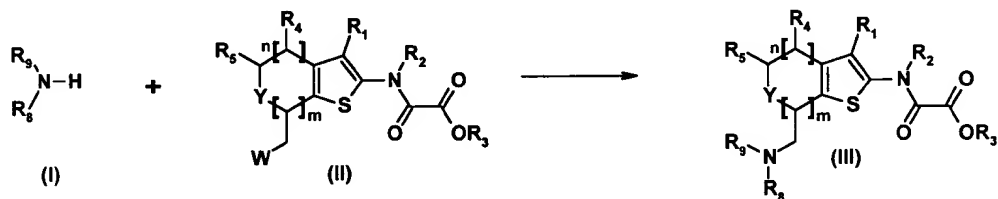
a) NCCH_2R_1 , sulphur, morpholine or triethylamine, EtOH; b) $\text{R}_3\text{OCOCOimidazole}$, THF; c) 25% TFA/ CH_2Cl_2 ;

B)



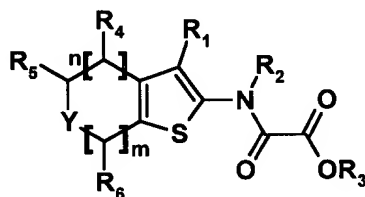
Allowing an amine (I) and a substituted oxalamide (II) to react under basic conditions or under Mitsunobu conditions to yield (III) wherein W is OH, OSO₂Me or halo;

C)



Allowing an amine (I) and a substituted oxalamide (II) to react under basic conditions or under Mitsunobu conditions to yield (III) where W is OH, OSO₂Me or halo.

143. (new) A compound of Formula 1



Formula 1

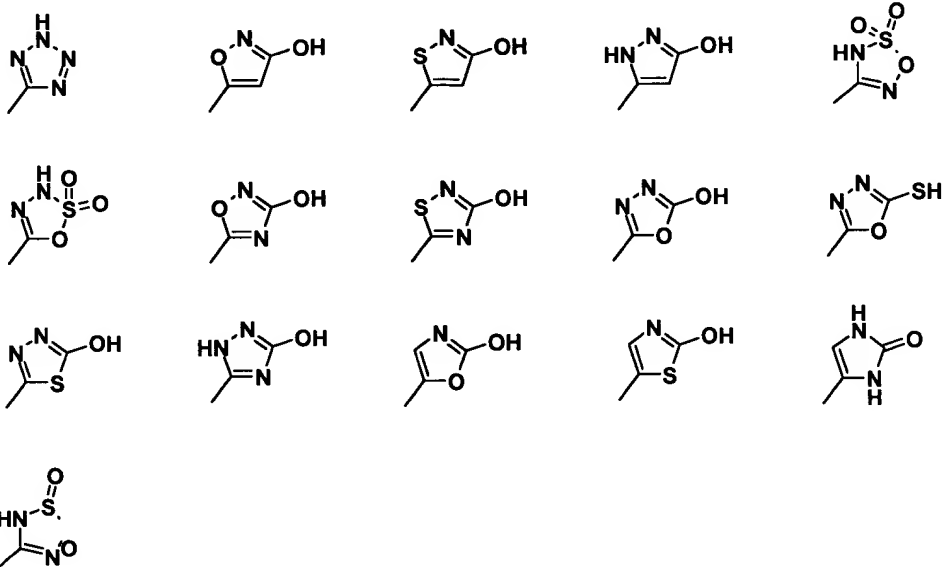
wherein

n is 1 or 2;

m is 1 or 2;

Y is O, S, SO or SO₂;

R₁ is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl or a 5-membered heterocycles selected from the group consisting of:



R₂ is hydrogen;

R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₄ is hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined below;

R₅ is C₁-C₆alkylNR₇R₈ wherein R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic monocyclic, bicyclic or tricyclic ring system selected from the group consisting of pyrrolopyrazin, pyrrolopyridine, benzo[d]isoxazole, 1,1-dioxo-1,3-dihydro-benzo[d]isothiazole, pyrrolidine and 1,3-dihydro-benzo[d]isothiazole substituted with two oxo groups at the atom positions adjacent to the nitrogen atom, wherein the ring system is optionally be substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, COOR₃, hydroxy, nitro, oxo, C₁-C₆alkyloxy,

arylC₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylaminoC₁-C₆alkyl or NR₉R₁₀, wherein R₉ and R₁₀ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted as defined below;

wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo, CONR₇R₈, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, NR₇R₈, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy, arylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-C₆alkylaminoCOR₁₂, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, -CONR₇R₈, -C₁-C₆alkylCONR₇R₈, or a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam, wherein R₁₂ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy;

and wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, COOR₃, CONR₇R₈, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkyl-aminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, carboxyC₁-C₆alkyloxy, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₇C₁-C₆alkylCOR₁₂, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -CONR₇R₈, or -C₁-C₆alkylCONR₇R₈;

R₆ is hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, oxo, carboxy, carboxyC₁-C₆alkyl, C₁-C₆alkyloxy-carbonyl, aryloxy-carbonyl, arylC₁-

C₆alkyloxycarbonyl, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₈R₉, C₁-C₆alkylaminoC₁-C₆alkyl, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxy, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkyl-carboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₈C₁-C₆alkylCOR₁₁, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, C₁-C₆alkylCONR₇R₈ or arylaminocarbonylaminoC₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined for R₅ and R₁₁ is NR₇R₈, or C₁-C₆alkylNR₇R₈;

R₇ and R₈ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy wherein the alkyl and aryl groups are optionally substituted as defined in the section of definitions; or R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic monocyclic, bicyclic or tricyclic ring system containing from 3 to 14 carbon atoms and from 0 to 3 additional heteroatoms selected from nitrogen, oxygen or sulphur, wherein the ring system is optionally substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylaminoC₁-C₆alkyl or NR₁₁R₁₂, wherein R₁₁ and R₁₂ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted as defined below; or

Wherein R₇ and R₈ are independently a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam;

wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo,

COOR₃, CONR₇R₈, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, NR₇R₈, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy, arylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-C₆alkylaminoCOR₁₃, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, -CONR₇R₈, -C₁-C₆alkylCONR₇R₈, or a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam, wherein R₁₃ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy;

and wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, CONR₇R₈, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₇C₁-C₆alkylCOR₁₃, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -CONR₇R₈, or -C₁-C₆alkylCONR₇R₈.

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.

144. (new) The compound according to claim 143, wherein the ring system is 1,3-dihydro-benzo[d]isothiazolyl, substituted with 2 oxo groups at the atom positions adjacent to the nitrogen atom.

145. (new) The compound according to claim 143, wherein the ring system is thiazolidin-2,4-dione.

146. (new) The compound according to claim 143, wherein the ring system is 5-(aryl-methyl)-thiazolidin-2,4-dione.

147. (new) The compound according to claim 143, wherein the ring system is pyrrolo[3,4-b]pyridine-5,7-dione.

148. (new) The compound according to claim 143, wherein the ring system is pyrrolo[3,4-b]pyridine-1,3-dione.

149. (new) The compound according to claim 143, wherein the ring system is pyrrolo[3,4-b]pyrazine-5,7-dione.

150. (new) A composition comprising an effective amount of a compound of claim 143, together with one or more pharmaceutically acceptable carriers or diluents and an insulin sensitizer.

151. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 143 and an insulin sensitizer.

152. (new) A composition comprising an effective amount of a compound of claim 143, together with one or more pharmaceutically acceptable carriers or diluents and an agent stimulating insulin release from β cells.

153. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need

thereof an effective amount of a compound of claim 143 and an agent stimulating insulin release from β cells.

154. (new) A composition comprising a compound of claim 143, together with one or more pharmaceutically acceptable carriers or diluents and an antiobesity agent.

155. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 143 and an antiobesity agent.

156. (new) A composition according to claim 150, wherein the insulin sensitizer is a thiazolidinedione or a pharmaceutically acceptable salt thereof.

157. (new) A composition according to claim 150, wherein the insulin sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione and 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salts thereof.

158. (new) A composition according to claim 150, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salts thereof.

159. (new) The method according to claim 151, wherein the insulin sensitizer is a thiazolidinedione or (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

160. (new) The method according to claim 151, wherein the insulin sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[4-[3-Methyl-4-

oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione or (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

161. (new) The method according to claim 151, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

162. (new) A composition according to claim 152, wherein the agent stimulating insulin release from β cells is repaglinide.

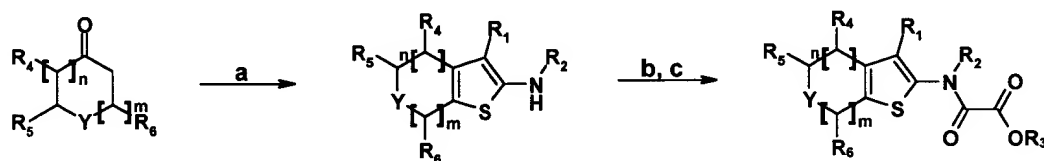
163. (new) The method according to claim 153, wherein the agent stimulating insulin release from β cells is repaglinide.

164. (new) A composition according to claim 154, wherein the antiobesity agent is orlistat.

165. (new) The method according to claim 155, wherein the antiobesity agent is orlistat.

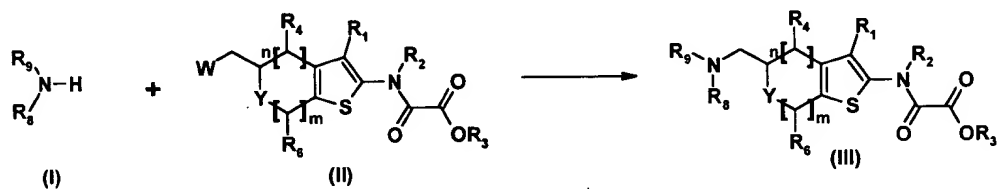
166. (new) A method for preparing the compound of claim 143, comprising

A)



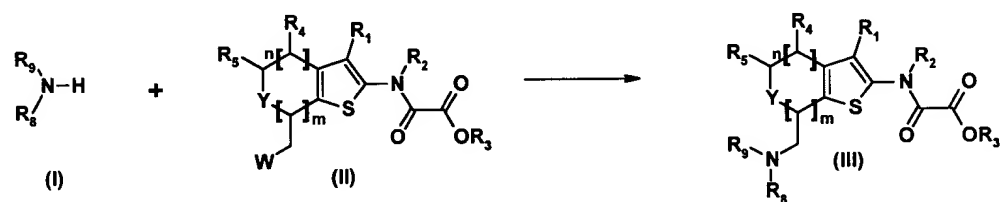
a) NCCH_2R_1 , sulphur, morpholine or triethylamine, EtOH; b) $\text{R}_3\text{OCOCOimidazole}$, THF; c) 25% TFA/ CH_2Cl_2 ;

B)



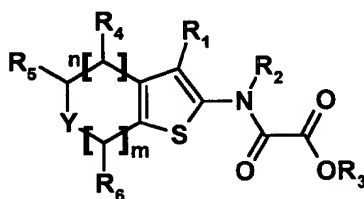
Allowing an amine (I) and a substituted oxalamide (II) to react under basic conditions or under Mitsunobu conditions to yield (III) wherein W is OH, OSO₂Me or halo;

C)



Allowing an amine (I) and a substituted oxalamide (II) to react under basic conditions or under Mitsunobu conditions to yield (III) where W is OH, OSO₂Me or halo.

167. (new) A compound of Formula 1



Formula 1

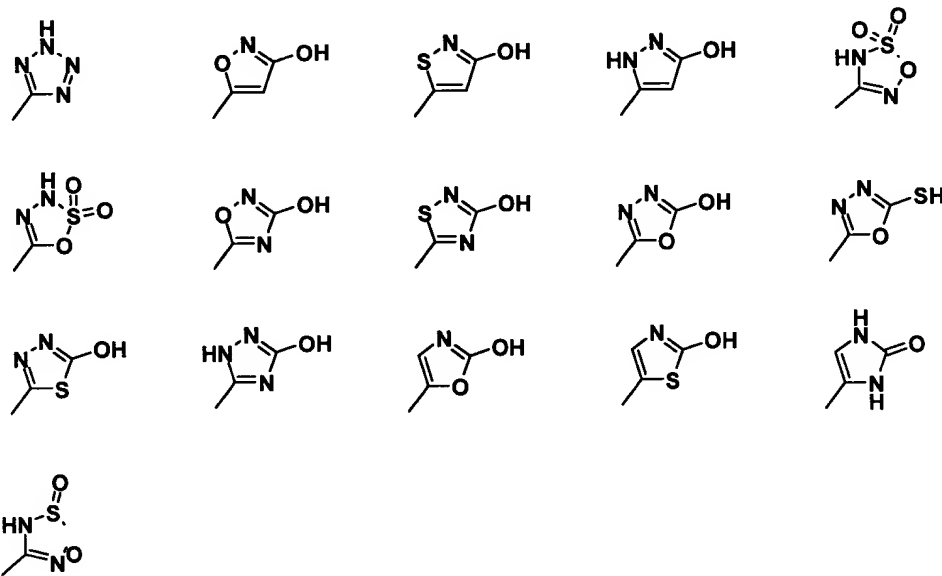
wherein

n is 1 or 2;

m is 1 or 2;

Y is O, S, SO or SO₂;

R_1 is COOH , $\text{COOC}_1\text{-C}_6\text{alkyl}$, $\text{COOarylC}_1\text{-C}_6\text{alkyl}$, $\text{COOC}_1\text{-C}_6\text{alkylcarbonyloxyC}_1\text{-C}_6\text{alkyl}$, $\text{COOC}_1\text{-C}_6\text{alkylcarbonyloxyarylC}_1\text{-C}_6\text{alkyl}$ or a 5-membered heterocycles selected from the group consisting of:



R_2 is hydrogen;

R_3 is hydrogen, $\text{C}_1\text{-C}_6\text{alkyl}$, $\text{arylC}_1\text{-C}_6\text{alkyl}$, $\text{C}_1\text{-C}_6\text{alkylcarbonyloxyC}_1\text{-C}_6\text{alkyl}$ or $\text{C}_1\text{-C}_6\text{alkylcarbonyloxyarylC}_1\text{-C}_6\text{alkyl}$;

R_4 is hydrogen, $\text{C}_1\text{-C}_6\text{alkyl}$, aryl , $\text{arylC}_1\text{-C}_6\text{alkyl}$; wherein the alkyl and aryl groups are optionally substituted as defined below;

R_5 is $\text{C}_1\text{-C}_6\text{alkylNR}_7\text{R}_8$ wherein R_7 and R_8 together with the nitrogen to which they are attached form isoindol wherein the ring system is optionally be substituted with at least one $\text{C}_1\text{-C}_6\text{alkyl}$, aryl , $\text{arylC}_1\text{-C}_6\text{alkyl}$, fluoro , hydroxy , oxo , $\text{C}_1\text{-C}_6\text{alkyloxy}$, $\text{arylC}_1\text{-C}_6\text{alkyloxy}$, $\text{C}_1\text{-C}_6\text{-alkyloxyC}_1\text{-C}_6\text{alkyl}$, $\text{C}_1\text{-C}_6\text{alkylamino-C}_1\text{-C}_6\text{alkyl}$ or NR_9R_{10} , wherein R_9 and R_{10} are independently selected from hydrogen, $\text{C}_1\text{-C}_6\text{alkyl}$, aryl , $\text{arylC}_1\text{-C}_6\text{alkyl}$,

C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted as defined below or optionally substituted with one chloro or six chloros;

wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo, COOR₃, CONR₇R₈, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, NR₇R₈, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy, arylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-C₆alkylaminoCOR₁₁, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, -CONR₇R₈, -C₁-C₆alkylCONR₇R₈, or a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam, wherein R₁₁ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy;

and wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, COOR₃, CONR₇R₈, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-

C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylthio, arylC₁-C₆alkylthio, NR₇R₈, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkyl-aminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, carboxyC₁-C₆alkyloxy, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₇C₁-C₆alkylCOR₁₂, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -CONR₇R₈, or -C₁-C₆alkylCONR₇R₈;

R₆ is hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, oxo, carboxy, carboxyC₁-C₆alkyl, C₁-C₆alkyloxycarbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₈R₉, C₁-

CI
C1
C6alkylaminoC₁-C₆alkyl, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxy, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₈C₁-C₆alkylCOR₁₂, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, C₁-C₆alkylCONR₇R₈ or arylaminocarbonylaminoC₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined for R₅ and R₁₂ is NR₇R₈, or C₁-C₆alkylNR₇R₈;

Wherein R₇ and R₈ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy wherein the alkyl and aryl groups are optionally substituted as defined in the section of definitions; or R₇ and R₈ together with the nitrogen to which they are attached form a saturated, partially saturated or aromatic monocyclic, bicyclic or tricyclic ring system containing from 3 to 14 carbon atoms and from 0 to 3 additional heteroatoms selected from nitrogen, oxygen or sulphur, wherein the ring system is optionally substituted with at least one C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylaminoC₁-C₆alkyl or NR₁₁R₁₂, wherein R₁₁ and R₁₂ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy; wherein the alkyl and aryl groups are optionally substituted as defined below; or R₇ and R₈ are independently a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam;

wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo, COOR₃, CONR₇R₈, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, NR₇R₈, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy, arylcarboxy, arylC₁-

C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-C₆alkylaminoCOR₁₃, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, -CONR₇R₈, -C₁-C₆alkylCONR₇R₈, or a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam, wherein R₁₃ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy;

and wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, CONR₇R₈, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₇C₁-C₆alkylCOR₁₃, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -CONR₇R₈, or -C₁-C₆alkylCONR₇R₈.

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.

168. (new) The compound of claim 167, wherein the ring system is optionally substituted with hydroxy, nitro, methoxy, benzyloxy, fluoro, chloro
CH₃CH₂CH₂NHC(O)- or CH₃C(O)NH.

169. (new) A composition comprising an effective amount of a compound of claim 167, together with one or more pharmaceutically acceptable carriers or diluents and an insulin sensitizer.

170. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 167 and an insulin sensitizer.

CI
171. (new) A composition comprising an effective amount of a compound of claim 167, together with one or more pharmaceutically acceptable carriers or diluents and an agent stimulating insulin release from β cells.

172. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 167 and an agent stimulating insulin release from β cells.

173. (new) A composition comprising a compound of claim 167, together with one or more pharmaceutically acceptable carriers or diluents and an antiobesity agent.

174. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 167 and an antiobesity agent.

175. (new) A composition according to claim 169, wherein the insulin sensitizer is a thiazolidinedione or a pharmaceutically acceptable salt thereof.

176. (new) A composition according to claim 169, wherein the insulin sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione and 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salts thereof.

177. (new) A composition according to claim 169, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salts thereof.

178. (new) The method according to claim 170, wherein the insulin sensitizer is a thiazolidinedione or (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

179. (new) The method according to claim 170, wherein the insulin sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione or (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

180. (new) The method according to claim 170, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

181. (new) A composition according to claim 171, wherein the agent stimulating insulin release from β cells is repaglinide.

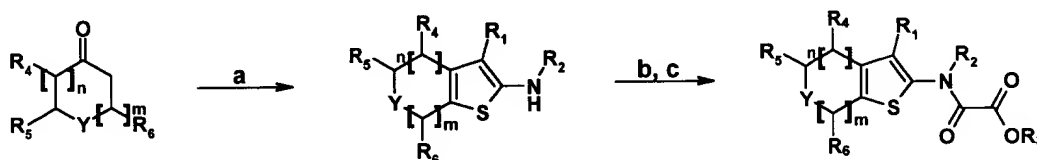
182. (new) The method according to claim 172, wherein the agent stimulating insulin release from β cells is repaglinide.

183. (new) A composition according to claim 173, wherein the antiobesity agent is orlistat.

184. (new) The method according to claim 174, wherein the antiobesity agent is orlistat.

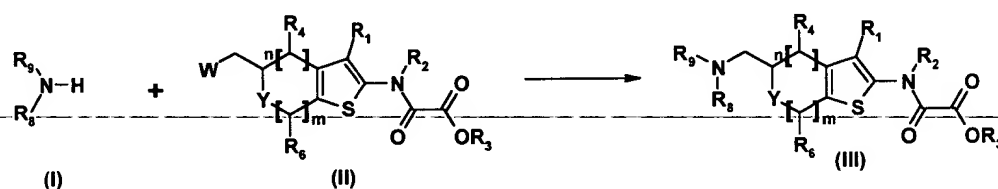
185. (new) A method for preparing the compound of claim 167, comprising

A)



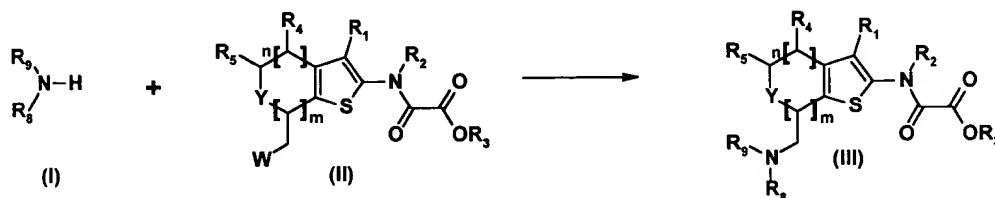
a) NCCH_2R_1 , sulphur, morpholine or triethylamine, EtOH; b) $\text{R}_3\text{OCOCOimidazole}$, THF; c) 25% TFA/ CH_2Cl_2 ;

B)



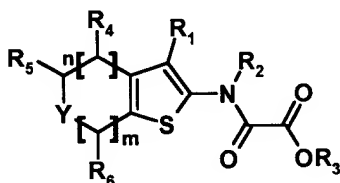
Allowing an amine (I) and a substituted oxalamide (II) to react under basic conditions or under Mitsunobu conditions to yield (III) wherein W is OH, OSO_2Me or halo;

C)



Allowing an amine (I) and a substituted oxalylamide (II) to react under basic conditions or under Mitsunobu conditions to yield (III) where W is OH, OSO₂Me or halo.

186. (New) A compound of Formula 1



Formula 1

wherein

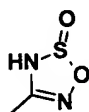
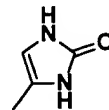
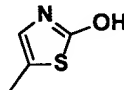
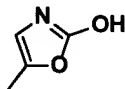
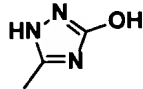
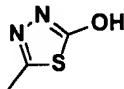
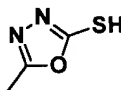
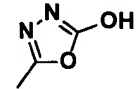
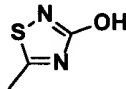
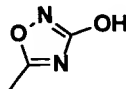
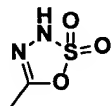
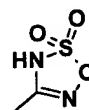
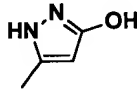
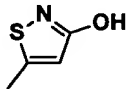
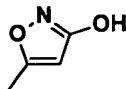
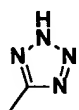
n is 1 or 2;

m is 1 or 2;

Y is O, S, SO or SO₂;

R₁ is COOH, COOC₁-C₆alkyl, COOarylC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyC₁-C₆alkyl, COOC₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl or a 5-membered heterocycles

selected from the group consisting of:



R₂ is hydrogen;

R₃ is hydrogen, C₁-C₆alkyl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyloxyC₁-C₆alkyl or C₁-C₆alkylcarbonyloxyarylC₁-C₆alkyl;

R₄ is hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined below;

R₅ is or C₁-C₆alkylNR₇R₈ or arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl,

R₆ is hydrogen, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, oxo, carboxy, carboxyC₁-C₆alkyl, C₁-C₆alkyloxycarbonyl, aryloxycarbonyl, arylC₁-C₆alkyloxycarbonyl, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxyC₁-C₆alkyl, arylC₁-C₆alkyloxyC₁-C₆alkyl, NR₇R₈, C₁-C₆alkylaminoC₁-C₆alkyl, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆=alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxyC₁-C₆alkyl, arylcarboxyC₁-C₆alkyl, arylC₁-C₆alkylcarboxyC₁-C₆alkyl, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₈C₁-C₆alkylCOR₁₁, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, CONR₇R₈, C₁-C₆alkylCONR₇R₈ or arylaminocarbonylaminoC₁-C₆alkyl; wherein the alkyl and aryl groups are optionally substituted as defined for R₅ and R₁₁ is NR₇R₈, or C₁-C₆alkylNR₇R₈;

R₇ and R₈ are independently selected from hydrogen, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkylcarbonyl, arylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkylcarboxy or arylC₁-C₆alkylcarboxy wherein the alkyl and aryl groups are optionally substituted as defined in the section of definitions; or R₇ and R₈ are independently a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam;

wherein the optionally substituted alkyl groups are substituted with one or more groups independently selected from halo, cyano, nitro, trihalomethyl, carbamoyl, hydroxy, oxo, COOR₃, CONR₇R₈, C₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy, NR₇R₈, C₁-C₆alkylamino, arylamino, arylC₁-C₆alkylamino, di(arylC₁-C₆alkyl)amino, C₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonyl, C₁-C₆alkyl-carboxy, arylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, -C₁-C₆alkylaminoCOR₁₂, arylC₁-C₆alkylcarbonylamino, tetrahydrofuranyl, morpholinyl, piperazinyl, -CONR₇R₈, -C₁-C₆alkylCONR₇R₈, or a saturated or partial saturated cyclic 5, 6 or 7 membered amine, imide or lactam, wherein R₁₂ is C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, C₁-C₆alkyloxy, aryloxy, arylC₁-C₆alkyloxy;

and wherein the optionally substituted aryl group is substituted with a group selected from halo, nitro, cyano, trihalomethyl, C₁-C₆alkyl, aryl, arylC₁-C₆alkyl, hydroxy, COOR₃, CONR₇R₈, C₁-C₆alkyloxy, C₁-C₆alkyloxyC₁-C₆alkyl, aryloxy, arylC₁-C₆alkyloxy, arylC₁-C₆alkyloxyC₁-C₆alkyl, C₁-C₆alkylthio, arylthio, arylC₁-C₆alkylthio, NR₇R₈, C₁-C₆alkylamino, C₁-C₆alkylaminoC₁-C₆alkyl, arylamino, arylC₁-C₆alkylamino, arylC₁-C₆alkylaminoC₁-C₆alkyl, di(arylC₁-C₆alkyl)aminoC₁-C₆alkyl, C₁-C₆alkylcarbonyl, C₁-C₆alkylcarbonylC₁-C₆alkyl, arylC₁-C₆alkylcarbonyl, arylC₁-C₆alkylcarbonylC₁-C₆alkyl, C₁-C₆alkylcarboxy, arylC₁-C₆alkylcarboxy, C₁-C₆alkylcarbonylamino, C₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -carbonylNR₇C₁-C₆alkylCOR₁₁, arylC₁-C₆alkylcarbonylamino, arylC₁-C₆alkylcarbonylaminoC₁-C₆alkyl, -CONR₇R₈, or -C₁-C₆alkylCONR₇R₈

and wherein aryl in R₅ is selected from the group consisting of phenyl, pyridyl, imidazolyl, benzo[1,3]dioxole, benzothiazolyl, biphenyl, indenyl, fluorenyl, naphthyl, pyrazolyl, triazolyl, oxazolyl, thiazolyl, quinolyl, pyrimidinyl, benzo[b]thiophenyl, benzothiazolyl, piperidinyl, pyrrolidinyl, phenylpyridyl, phenylpyrimidyl, benzothiazolyl, carbazolyl,

or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, a racemic mixture, or any tautomeric form, or prodrug thereof.

187. (new) The compound according to claim 186, wherein R_1 is COOH , $\text{COOC}_1\text{-C}_6\text{alkyl}$, $\text{COOarylC}_1\text{-C}_6\text{alkyl}$, $\text{COOC}_1\text{-C}_6\text{alkylcarbonyloxyC}_1\text{-C}_6\text{alkyl}$, $\text{COOC}_1\text{-C}_6\text{alkylcarbonyloxyarylC}_1\text{-C}_6\text{alkyl}$.

188. (new) The compound according to claim 186, wherein n and m are 1.

189. (new) The compound according to claim 186, wherein Y is oxygen.

190. (new) The compound according to claim 186, wherein R_1 is 5-tetrazolyl, R_5 is $\text{C}_1\text{-C}_6\text{alkylNR}_7\text{R}_8$ and Y is oxygen.

191. (new) The compound according to claim 186, wherein R_4 and R_6 are hydrogen.

192. (new) The compound according to claim 186, wherein R_6 is $\text{C}_1\text{-C}_6\text{alkylNR}_7\text{R}_8$.

193. (new) The compound according to claim 186, wherein the aryl group is pyridyl.

194. (new) The compound according to claim 186, wherein the aryl group is phenyl optionally substituted with methoxy or $\text{CH}_3\text{C(O)}$.

195. (new) The compound according to claim 186, wherein R_7 is hydrogen and R_8 is $\text{C}_1\text{-C}_6\text{alkylaryl}$.

196. (new) The compound according to claim 186, wherein R_6 is arylaminocarbonylamino $\text{C}_1\text{-C}_6\text{alkyl}$.

197. (new) The compound according to claim 186, wherein R₆ is aryloxyC₁-C₆alkyl.

198. (new) The compound according to claim 186, wherein the aryl group is 1,1-dioxo-benzo[d]isothiazol-3-yl.

199. (new) the compound according to claim 186, wherein the aryl group is 1,1-dioxo-5-phenyl-isothiazol-3-yl.

200. (new) The compound according to claim 186, wherein the aryl group is benzo[1,3]dioxol-5-yl.

201. (new) The compound according to claim 186, wherein the aryl group is 5-methoxy-2-methyl-1H-indol-3-yl.

202. (new) A composition comprising an effective amount of a compound of claim 186, together with one or more pharmaceutically acceptable carriers or diluents and an insulin sensitizer.

203. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 186 and an insulin sensitizer.

204. (new) A composition comprising an effective amount of a compound of claim 186, together with one or more pharmaceutically acceptable carriers or diluents and an agent stimulating insulin release from β cells.

205. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need

thereof an effective amount of a compound of claim 186 and an agent stimulating insulin release from β cells.

206. (new) A composition comprising a compound of claim 186, together with one or more pharmaceutically acceptable carriers or diluents and an antiobesity agent.

207. (new) A method of treating type I diabetes, type II diabetes, impaired glucose tolerance, insulin resistance or obesity comprising administering to a subject in need thereof an effective amount of a compound of claim 187 and an antiobesity agent.

208. (new) A composition according to claim 202, wherein the insulin sensitizer is a thiazolidinedione or a pharmaceutically acceptable salt thereof.

209. (new) A composition according to claim 202, wherein the insulin sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[[4-[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl-methyl]thiazolidine-2,4-dione and 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salts thereof.

210. (new) A composition according to claim 202, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

211. (new) The method according to claim 203, wherein the insulin sensitizer is a thiazolidinedione or (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

212. (new) The method according to claim 203, wherein the insulin sensitizer is selected from troglitazone, ciglitazone, pioglitazone, rosiglitazone, 5-[[4-[3-Methyl-4-

oxo-3,4-dihydro-2-quinazoliny]methoxy]phenyl-methyl]thiazolidine-2,4-dione or (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

213. (new) The method according to claim 203, wherein the insulin sensitizer is (-) 3-[4-[2-Phenoxazin-10-yl)ethoxy]phenyl]-2-ethoxypropanoic acid or a pharmaceutically acceptable salt thereof.

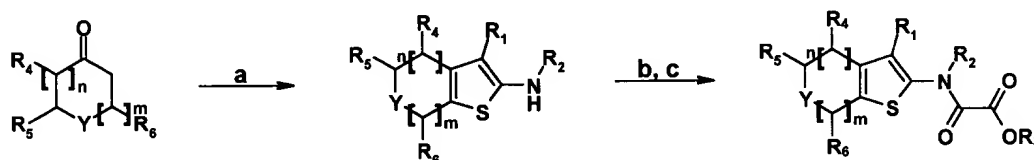
214. (new) A composition according to claim 204, wherein the agent stimulating insulin release from β cells is repaglinide.

215. (new) The method according to claim 205, wherein the agent stimulating insulin release from β cells is repaglinide.

216. (new) A composition according to claim 206, wherein the antiobesity agent is orlistat.

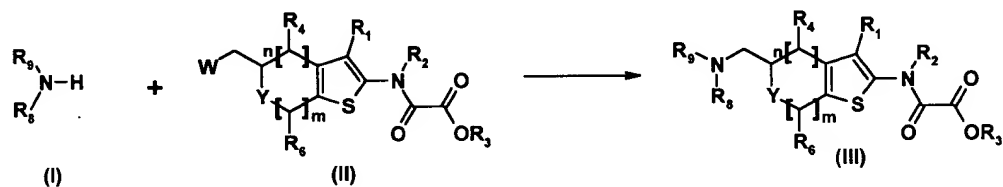
217. (new) The method according to claim 209, wherein the antiobesity agent is orlistat.

218. (new) A method for preparing the compound of claim 186, comprising
A)



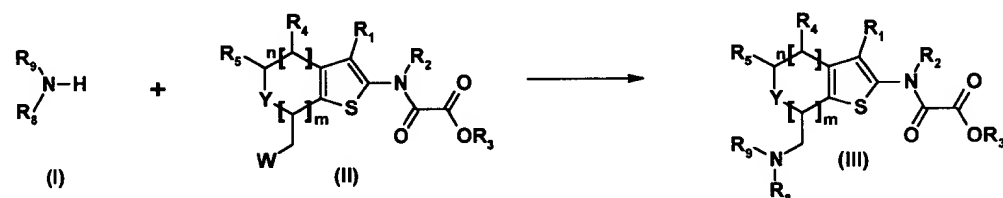
a) NCCH_2R_1 , sulphur, morpholine or triethylamine, EtOH; b) $\text{R}_3\text{OCOCOimidazole}$, THF; c) 25% TFA/ CH_2Cl_2 ;

B)



Allowing an amine (I) and a substituted oxalylamide (II) to react under basic conditions or under Mitsunobu conditions to yield (III) wherein W is OH, OSO₂Me or halo;

C)



Allowing an amine (I) and a substituted oxalylamide (II) to react under basic conditions or under Mitsunobu conditions to yield (III) where W is OH, OSO₂Me or halo.

219. (new) A compound which acts as an inhibitor of Protein Tyrosine Phosphatases selected from the group consisting of

2-(Oxalyl-amino) (1,1,3-trioxo-1,3-dihydro-1H-benzo[d]isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran carboxylic acid;

5-(4-Chloro-1,3-dioxo-1,3-dihydro-isoindol-2-yl-methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4,5,6,7-Tetrachloro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Methoxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

C1
Contd

5-(4-Hydroxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Benzoyloxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Fluoro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(1,3-Dioxo-1,3-dihydro-benzo[f]isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Acetyl-amino-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Acetyl-amino-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-b]pyrazin-6-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-b]pyridin-6-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5,7-Dioxo-5,7-dihydro-pyrrolo[3,4-c]pyridin-6-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Nitro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Hydroxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Methoxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-Nitro-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(4-(4-Chloro-phenyl)sulfanyl)-6-methyl-1,3-dioxo-1,3-dihydro-pyrrolo[3,4-c]pyridin-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(3-Imidazol-1-yl-2,5-dioxo-pyrrolidin-1-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

Oxalic acid 3-carboxy-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-5-ylmethyl ester methyl;

Oxalic acid (3-carboxy-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-5-ylmethyl) ester;

7-Hydroxymethyl-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(2,4-Dioxo-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylloxymethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(4-Hydroxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Methoxy-1,3-dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5,7-Dioxo-5,7-dihydro-[1,3]dioxolo[4,5-f]isoindol-6-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(((Benzo[1,3]dioxole carbonyl)amino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(3-(2,4-Dimethoxy-phenyl)ureidomethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-5-phenylcarbamoyl-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-Benzylcarbamoyl-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3,7-dicarboxylic acid 7-ethyl ester;

7-Benzylcarbamoyl-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-((2-(4-Methanesulfonyl-phenyl)-acetylamino)-methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-((3-Carboxy-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-5-ylmethyl)-carbamoyl)nicotinic acid;

7-(2,4-Dioxo-5-pyridin-2-ylmethylene-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(2,4-Dioxo-5-pyridin-ylmethyl-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5-(4-Methoxy-benzylidene)-2,4-dioxo-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5-(4-Acetylamino-benzylidene)-2,4-dioxo-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(5-(3,5-Dimethoxy-benzylidene)-2,4-dioxo-thiazolidin-3-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-[5-(1H-Imidazol-4(5)-ylmethylene)-2,4-dioxo-thiazolidin-3-ylmethyl]-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(1,3-Dioxo-4,7-epoxido-1,3,4,5,6,7-hexahydro-isoindol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(((2R)-Amino-3-phenyl-propionylamino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-((2-Acetylamino-3-(4-hydroxy-phenyl)-propionylamino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-((2-Acetylamino-3-methyl-butyrylamino)methyl)-3-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-7-(1,1,3-trioxo-1,3-dihydro-1H-benzo[d]isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-7-(1,1,3-trioxo-1H-benzo[d]isothiazol-3-ylloxomethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-7-(3-oxo-3H-benzo[d]isoxazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-7-(1,1,3-trioxo-5-phenyl-1,3-dihydro-isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(1,1-Dioxo-5-phenyl-1H-isothiazol-3-ylloxymethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-5-(1,1,3-trioxo-5-phenyl-1,3-dihydro-isothiazol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(1,1-Dioxo-5-phenyl-1H-isothiazol-3-ylloxymethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(6-Chloro-1,1,3-trioxo-2,3-dihydro-4H-thieno[3,2-e]-1,2,4-thiadiazin-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(6-Chloro-1,1-dioxo-4H-thieno[3,2-e]-1,2,4-thiadiazine-3-ylloxymethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

7-(1,3-Dioxo-1,3-dihydro-benzo[d]isothiazol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran carboxylic acid;

5-(1,3-Dioxo-1,3-dihydro-benzo[d]isothiazol-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Benzyl-1,1-dioxo-[1,2,5]thiadiazolidin-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(5-Ethyl-1,1-dioxo-[1,2,5]thiadiazolidin-2-ylmethyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-7-(1-oxo-1,3-dihydro-isoindol-2-ylmethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

2-(Oxalyl-amino)-5-(2,2,2-trifluoro-acetoxymethyl)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-(((Benzo[1,3]dioxol-5-ylmethyl)-amino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-((2-Methoxy-benzylamino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;

5-((2-Benzo[1,3]dioxol-yl-acetylamino)methyl)-2-(oxalyl-amino)-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid;